UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/554,410	11/17/2005	Giovanni Paganelli	GRT/4865-17	4581

23117 7590 11/26/2007

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
GUSSOW, ANNE	
ART UNIT	**PAPER NUMBER**
1643	

MAIL DATE	DELIVERY MODE
11/26/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/554,410	PAGANELLI ET AL.	
	Examiner	Art Unit	
	Anne M. Gussow	1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 October 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 17-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 17-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/05, 10/2/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election of Group II, claims 1-14, and 17 in the reply filed on October 2, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 15-16 have been cancelled.

Claims 1-14 and 17 have been amended.

Claims 18-22 have been added.

3. Claims 1-14 and 17-22 are under examination.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file. Should applicant desire to obtain the benefit of foreign priority under 35 U.S.C. 119(a)-(d), a certified English translation of the foreign application must be submitted in reply to this action. 37 CFR 41.154(b) and 41.202(e).

Failure to provide a certified translation may result in no benefit being accorded for the non-English application.

Due to the priority document being in a foreign language the claims receive the priority date of April 7, 2004 for art rejection purposes in this office action.

Information Disclosure Statement

5. The listing of references in the specification is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered.

6. The information disclosure statements (IDS) submitted on October 24, 2005 and October 2, 2007 have been fully considered by the examiner and an initialed copy of the IDS is included with the mailing of this Office Action.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 1-14, and 17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims are vague and indefinite for reciting the phrase "endowed with tumor tropism" in claim 1. It is not clear what endowed with tumor tropism means in relation to the agent. The American Heritage Dictionary (2006) defines endow as to equip or supply with a talent or quality, to imagine as having a usually favorable trait or quality. It is not clear how the agent is endowed with tumor tropism, is it an inherent property or is a method required to endow the agent?

Claim Rejections - 35 USC § 102

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3-8, 10-13, 17, 18, and 20-22 are rejected under 35 U.S.C. 102(b) as being anticipated by Goldenberg (US PG PUB 2001/0006618, published July 5, 2001).

The claims recite a method of treating a patient with a solid tumor, said method comprising administering to said patient a first agent endowed with tumor tropism in combination with a second anticancer agent with affinity for said first agent, in which said first agent is avidin and said second anticancer agent is a biotinylated anticancer agent, in which said second anticancer agent comprises an anticancer agent, in which said anticancer agent is a radioisotope, in which said radioisotope is Y-90 or Lu-177, in which said first agent and said second anticancer agent are administered separately, in which said first agent is selected from the group consisting of avidin, streptavidin, their

polymeric derivatives and their derivatives with polyethylene glycol, in which said first agent and second anticancer agent are administered by injection, in which said first agent is administered in a single dose. The claims also recite a method of diagnosing cancer in a patient, said method comprising administering to said patient a first agent endowed with tumor tropism in combination with a second radiolabeled agent endowed with affinity for said first agent for diagnosis by determining the pretherapeutic biodistribution of the tumor in the patient. The claims also recite a method of treating a patient with a solid tumor, said method comprising: (a) administering to the patient, who is undergoing surgery, a first agent with affinity for the solid tumor directly to said solid tumor exposed during surgery or an anatomical area containing said solid tumor after surgical removal of the cancer and then (b) systemically administering to the patient, who has undergone surgery, a second anticancer agent with affinity for said first agent; thereby concentrating said second anticancer agent in the solid tumor or the anatomical area, in which said first agent is avidin and said second anticancer agent is a biotinylated and radiolabeled antibody, in which said first agent is selected from the group consisting of avidin, streptavidin, their polymeric derivatives and their derivatives with polyethylene glycol, in which said second anticancer agent comprises an anticancer agent selected from the group consisting of radioisotopes, chemotherapeutic agents, toxins and anticancer cells.

Goldenberg teaches a method for treating tumor by injecting a patient with a first agent comprising an avidin- or biotin-conjugated antibody which binds to a marker produced by or associated with the lesion and a second agent comprising either avidin

or biotin and a radiolabel (paragraphs 36 and 61). Goldenberg teaches suitable radiolabels to include Yittruim-90 (paragraph 114). Goldenberg teaches dosing the first and second agents 24 hours apart (paragraph 133). Goldenberg teaches the method can be used for detecting tumors intraoperatively in cecal carcinoma patients, thus diagnosing the location of tumor cells (see example 1). Since the claims do not recite the specific solid tumor for treatment or diagnosis and due to the indefinite nature of the term "endowed" (see 112, second paragraph, above), all the limitations of the claims have been met.

Claim Rejections - 35 USC § 103

11. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

12. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

13. Claims 1-13 and 17-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg (US PG PUB 2001/0006618, published July 5, 2001) in view of Cokgor, et al. (Journal of Clinical Oncology, 2000. Vol. 18, pages 3862-3872).

Claims 1, 3-8, 10-13, 17, 18, and 20-22 have been described supra. Claims 2, 9, and 19 recite a method of treating a patient with a solid tumor, said method comprising administering to said patient a first agent endowed with tumor tropism in combination with a second anticancer agent with affinity for said first agent, in which said first agent is administered during an intraoperative step via the locoregional route and said second anticancer agent is administered during a postoperative step via the systemic route, in which said solid tumor is selected from the group consisting of breast, pancreas, lung, pleural, peritoneal, cervico-facial, brain and bladder tumors.

Goldenberg has been described supra. Goldenberg, et al. do not teach locoregional administration of the first agent. Goldenberg, et al, do not teach treatment of breast, pancreas, lung, pleural, peritoneal, cervico-facial brain or bladder tumors. These deficiencies are made up for in the teachings of Cokgor, et al.

Cokgor, et al teach administration of radiolabeled 81C6 antibody directly to the surgical resection cavity in patients with malignant gliomas.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the cancer treatment agent of Goldenberg in the administration method as taught by Cokgor, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the treatment agent of Goldenberg in

the administration method of Cokgor, et al. because Cokgor, et al. teach that systemically administered antibodies are not as effective in the treatment of brain tumors because antibodies do not cross the blood brain barrier well and there is high interstitial fluid pressure in the tumor and surrounding normal tissue. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the agent of Goldenberg in the administration method of Cokgor, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

14. Claims 1, 3-8, 10-14, 17, 18, and 20-22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Goldenberg (US PG PUB 2001/0006618, published July 5, 2001) in view of Stendel, et al. (Anticancer Research, 2004. Vol. 24, pages 631-638).

Claims 1, 3-8, 10-13, 17, 18, and 20-22 have been described supra. Claim 14 recites the method of treating a patient with a solid tumor in which said first agent is administered by spray.

Goldenberg has been described supra. Goldenberg does not teach spray administration of the agent. This deficiency is made up for in the teachings of Stendel, et al.

Stendel, et al. teach spray administration of a taurolidine-fibrin-matrix directly into the surgical resection cavity of a brain tumor.

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the agent of Goldenberg in the spray administration method as taught by Stendel, et al.

One of ordinary skill in the art would have been motivated to and had a reasonable expectation of success to have used the agent of Goldenberg in the spray administration method as taught by Stendel, et al. because Stendel, et al. teach direct administration of a chemotherapy agent increases the concentration of the agent within the tumor site and results in lower concentration in other tissues compared to systemic administration. Thus, it would have been obvious to one of ordinary skill in the art at the time the claimed invention was made to have used the agent of Goldenberg in a spray administration method to treat tumors in view of Stendel, et al.

Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made, as evidenced by the references.

Conclusion

15. No claims are allowed.

16. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne M. Gussow whose telephone number is (571) 272-6047. The examiner can normally be reached on Monday - Friday 8:30 am - 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Anne M. Gussow

November 20, 2007

LARRY R. HELMS, PH.D.
SUPERVISORY PATENT EXAMINER